REMARKS

Status of the Claims

Claims 1-2, 4-13, 15, 17-18, and 20 will be pending in the above-identified application upon entry of the present amendment. Claims 12-13 are currently withdrawn from consideration. As such, claims 1-2, 4-11, 15, 17-18, and 20 stand ready for further action on the merits. Claims 5-6 and 8 have been amended. Claims 16 and 19 have been cancelled herein. No new matter has been added.

Applicant submits that the present Amendment is merely formal in nature, presents no new issues, reduces the number of issues under consideration, and places the case in condition for allowance. Alternatively, entry of the present amendment is proper to place the claims in better form for appeal.

In view of the following remarks, Applicant respectfully requests that the Examiner withdraw all rejections and allow the currently pending claims.

Information Disclosure Citation

Applicant thanks the Examiner for considering the references supplied with the Information Disclosure Statement filed March 26, 2010 and for providing Applicant with an initialed copy of the PTO-SB08 form filed therewith.

Issues under 35 U.S.C. § 112, second paragraph

Claims 1-2, 4-11, and 15-20 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite. Specifically, the Examiner asserts that it is unclear whether claim 1 is reciting components of a kit or whether the claim is drawn to a composition. Applicant respectfully traverses.

As described in the present specification, the present invention is a composition. The user does not receive two gels which have to be mixed for obtaining the final gel. Claim 1 clearly indicates what the components of the composition are, and one of ordinary skill in the art would understand that the final composition includes a mixture of all the components, including each one of the previously manufactured barrier gels. For these reasons, Applicant respectfully requests that the rejection be withdrawn.

Claim Objections

Claim 8 is objected to because the fourth and fifth lines of claim 8 are duplicates. Claim 16 is objected to for being a substantial duplicate of claim 5. Claim 19 is objected to for being a substantial duplicate of claim 6.

Claim 8 has been amended herein to overcome this objection. Claims 16 and 19 have been cancelled herein, which renders the objection moot. As such, Applicant respectfully requests that the objections be withdrawn.

Issues under 35 U.S.C. § 103(a)

1) Claims 1-2, 4-10, and 15-20 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Klein '918 (US 5,980,918) in view of Parrilla '838 (US 5,024,838), Beitner '171 (US 4,777,171), and Chen '182 (US 2003/01700182).

2) Claim 11 is rejected under 35 U.S.C. § 103(a) as being unpatentable over Klein '918 in view of Parrilla '838, Beitner '171, Chen '182, and Lezdey et al. '020 (US 6,262,020).

3) Claims 1-2, 4-10, and 15-20 are rejected under 35 U.S.C. § 103(a) as being unpatentable over CO '011 (CO 96/007011) in view of Beitner '171 and Chen '182.

4) Claim 11 is rejected under 35 U.S.C. § 103(a) as being unpatentable over CO '011 in view of Beitner '171 and Chen '182 and further in view of Lezdey et al. '020.

Applicant respectfully traverses. Reconsideration and withdrawal of these rejections are respectfully requested based on the following considerations.

Legal Standard for Determining Prima Facie Obviousness

MPEP 2141 sets forth the guidelines in determining obviousness. First, the Examiner has to take into account the factual inquiries set forth in *Graham v. John Deere*, 383 U.S. 1, 17, 148 USPQ 459, 467 (1966), which has provided the controlling framework for an obviousness analysis. The four *Graham* factors are:

(a) determining the scope and content of the prior art;

(b) ascertaining the differences between the prior art and the claims in issue;

(c) resolving the level of ordinary skill in the pertinent art; and

(d) evaluating any evidence of secondary considerations.

Graham v. John Deere, 383 U.S. 1, 17, 148 USPQ 459, 467 (1966).

Second, the Examiner has to provide some rationale for determining obviousness. MPEP 2143 sets forth some rationales that were established in the recent decision of *KSR International Co. v Teleflex Inc.*, 82 USPQ2d 1385 (U.S. 2007).

As the MPEP directs, all claim limitations must be considered in view of the cited prior art in order to establish a *prima facie* case of obviousness. *See* MPEP 2143.03.

Distinctions over Klein '918 in view of the secondary references

The present invention provides unexpected improvements over the prior art by creating two protective gel barriers which are prepared separately. The first protective gel barrier is composed of carboxypolymethylene, (e.g. in an amount of 1.5 - 2.5 wt %) in an aqueous vehicle with an emulsifier (e.g. triethanolamine). Carboxypolymethylene is a high-molecular weight synthetic resin (i.e. polymer matrix), which is polymerized with a hydrophobic monomer, thus obtaining an acrylic or polyacrylic acid polymer.

The carboxypolymethylene maintains the homogeneity of the preparations by stabilizing emulsified systems against sedimentation or separation, and by absorbing the respective interface. The carboxypolymethylene also is a thickener that increases the viscosity of solutions.

The present invention has the unexpected advantages of efficiently forming the protecting barrier, cleaning undesired oily substances, evenly distributing the preparation over the skin and accelerating the stabilization of the protective gel barrier. The composition of the invention is further translucent, does not cause skin irritation and is non-toxic. It further coalesces rapidly the application of the product, giving it consistency.

The second protective gel barrier of the instant invention, is composed of thickening agent, such as carboxymethylcellulose (CMC) (in, e.g. an amount of 1 - 4 wt %), and a preservative (e.g. parabene) in an aqueous vehicle. Sodium CMC is the sodium salt of a cellulose polycarboxymethyl ether, a high viscosity water-soluble anionic polymer. The CMC in the composition functions as a high quality thickener, which is compatible with other colloids, electrolytes, alcohols, etc. In addition, the CMC is easily dissolved in cold or warm water and is a dispersion suspending stabilizing agent. Further the CMC retains water contributing to the

dryness of the underlying injury and acts as a film-generating agent resistant to oils, greases, and organic solvents. It also acts as a binding agent and protective colloid.

The CMC also acts as a rheologic agent, i.e., it regulates flow properties, and has binding, emulsifying, dispersing, and agglutinant properties. It does not coagulate with heating below 40°C. CMC shows resistance to microbiological attacks, stability within a pH range of 4 to 9, being ideal at neutral pH, and is physiologically inert, an essential property for the desired effect.

The mixture of the two protective gel barriers constructs a topical gel composition having unexpected advantageous properties for the treatment of superficial burns and skin injuries.

The composition of the invention utilizes a proteolytic enzyme because of its exclusive dead tissue debridating action that respects healthy ones, an ideal action for the treatment of skin injuries.

The composition of the invention also uses an anesthetic for the immediate or mediate application of the composition, thus avoiding pain and stress, namely, one of current priorities in the treatment of superficial skin injuries or burns.

The composition of the invention also uses chlorohexidine as an antiseptic because of its bactericidal, bacteriostatic, and non-toxic properties. Chlorhexidine is free of bacterial resistance, active against skin bacteria, can be used in an aqueous solution, is non-irritant, with persistent antibacterial activity on the skin; as well as being quick acting, with minimum absorption, and does not delay wound healing.

The composition of the invention creates a protective gel shell (through the combination of the first and second barrier gels) combined with the debridating effects of the proteolytic enzyme, the antibacterial properties, and the comfort and analgesia provided by the anesthetic.

The composition may be applied immediately or mediately and proves beneficial in superficial skin injuries at the beginning of the tissue regeneration process for abrasions, superficial burns, chemical burns, avulsions, viral skin injuries, non-secreting infectious skin injuries, surgical wounds, dermal abrasions, and as an adjuvant in the treatment of deeper injuries.

The present inventive composition is both novel and unobvious over the prior art and presents a composition having the advantages of:

- promoting ideal conditions for the regeneration of skin epithelia.

- removing both debris and necrotic tissues.
- preventing tissue mistreatment because it does not adhere to the injury
- suppressing pain and stress to the patient, thus preventing autonomic, somatic, and endocrine responses.
- suppressing local pain at the injury though two mechanisms: i.e. by covering nerve endings, and though an analgesic action
- creating a protective defense barrier for the body, thus isolating injuries from contamination sources
- preventing the accumulation of secretions in the injury
- preventing wound dehydration due to water evaporation
- removing bacteria by virtue of its antiseptic component
- promoting rapid epithelialization, thus decreasing the formation of scars.

Klein - Klein teaches a topical composition for the treatment of burns, injuries, and scars, wherein the active ingredient is a cereal-derived (1-3) (1-4) ß-D-glycan. More particularly, the composition of Klein is related to topical cream and gel formulations with cleansing, hydrating, softening, and anti-pruriginous activities for the topical treatment of burns, wounds, and other skin injuries and conditions.

Klein uses carboxypolymethylene as a vehicle without any specific therapeutic function. In the description of the reference of gels it is used at 0.5%, whereas the instant composition of claim 5 uses it at 1.5% - 2.5% with a therapeutic action.

The components in Klein are all mixed to create creams and gels, whereas with the present invention two barrier gels are required, which each have different required components. In addition, with the Klein composition both triethanolamine and parabenes are used as stabilizers and preparation preservatives.

Klein fails teach or suggest a composition having the advantages that are associated with the present invention as dicussed above. Specifically, Klein fails to teach or suggest a composition that provides ideal conditions for skin epithelium regeneration; removes both debris and necrotic tissues; suppresses pain and thus prevents stress to the patient, which in turn prevents autonomic, somatic, and endocrine responses. Klein neither teaches nor suggests a

composition that suppresses local pain in the injury by 1) covering nerve endings and 2) analgesic action. Nor does Klein teach or suggest the creation of a protecting defense barrier for the body, isolating the injury from contamination sources, preventing the accumulation of secretions in the injury, removing bacteria by virtue of an antiseptic component or creating a rapid epithelialization process, thus decreasing scar formation.

Thus, there is no disclosure or suggestion in Klein regarding a composition composed of two barrier gels nor of the advantages associated therewith.

Parrilla - Parrilla fails to make up for the deficiencies of Klein. Parrilla discloses a composition for the treatment of skin injuries, such as burns. The composition of Parrilla is a film used to isolate and protect injuries and includes an antiseptic (benzalkonium chloride), a sapogenin (filiferin), and a proteolytic enzyme (papain), in a suitable hydrophilic colloid vehicle based on carboxymethylcellulose.

The composition of Parrilla prevents external stimulation because it is in contact with the nerve endings of the injury, thus suppressing pain. The physical barrier prevents the passage of microorganisms that may contaminate the wound. The antiseptic cleans the wound of any existing microorganisms. It reinforces proteolysis and accelerates the biochemical debridement processes.

However, as discussed above, the composition of the invention requires two protective barrier gels that together form a composition that create an isolating shell, i.e. a protecting defense barrier for the body. The first barrier gel of the invention maintains the homogeneity of the preparations, stabilizes the emulsified system, absorbs the respective interface, helps efficiently form the protecting barrier, cleans undesired oily substances, distributes evenly the preparation over the skin, accelerates the stabilization of the protective gel barrier, is translucent, does not cause skin irritation, is non-toxic, and coalesces very quickly upon the application of the product, thus giving it consistency. The second barrier gel is a thickener, compatible with other colloids, electrolytes, alcohols etc, and also a dispersion stabilizer, and a water retaining agent that contributes to the dryness of the underlying injury. It acts as a film-generating agent which is resistant to oils, greases, and organic solvents; it also acts as a binder and is a protective

colloid, which acts as rheologic agent, i.e. regulates flow properties, and is resistant to microbiological attacks.

The composition of the invention provides analgesia not only by covering nerve endings but also with the use of a local anesthetic, such as lidocaine; thus, suppressing pain produced by chemical substances from inflammation and ischemia (histamine, serotonin, etc.), which is described as nociceptive pain and which causes autonomic, somatic, and endocrine responses.

The composition of the invention not only succeeds in preventing the passages of contaminating microorganisms through protective barrier gels, but also provides improved antiseptic and anti-infective advantages. Benzalkonium chloride, which is used in Parrilla, is only moderately efficient as an antiseptic, and it is removed very quickly from surfaces and becomes contaminated very rapidly. In addition, toxicity has been described with benzalkonium in aquatic environments.

On the other hand, chlorhexidine, the specific antiseptic of the presently claimed composition, has important advantages, such as being an efficient bactericidal and/or bacteriostatic agent, non-toxic, free of bacterial resistance, active against skin bacteria, useful in aqueous solution, non-irritant, with persistent antibacterial activity on the skin, and a rapid onset of action, minimum absorption and chlorhexidine does not delay wound healing.

Parrilla's composition shows the therapeutic value of proteolytic enzymes in superficial non-infected skin injuries. The prior art composition accelerates the debridement process, thus making the environment less apt for bacterial colonization through removing debris and shortening epithelialization time. Thus, Parrilla teaches the use of a proteolytic enzyme for tissue debridement to prevent the occurrence of infections, but it is not indicated to treat infection once it occurs and and is not specific to remove bacteria.

Parrilla fails to teach or suggest a composition having two barrier gels that allows for the formation of an isolating shell, i.e. a protecting defense barrier for the body. Parrilla similarly fails to teach the advantages of the invention of a composition that suppresses inflammatory nociceptive pain, prevents stress to the patient and his/her tissues, and thus avoids autonomic, somatic, and endocrine responses; suppresses local pain in the injury by the mechanism of analgesic action of an anesthetic agent; removes bacteria and disinfects the wound through the

use of a highly bactericidal and bacteriostatic non-toxic antiseptic component. Thus, as note above, Parrilla fails to teach the deficiencies that are found in Klein.

Beitner - Beitner similarly fails to make up for the deficiencies of Klein and/or Parrilla so as to teach or suggest the instant invention. Beitner teaches the topical use of psychiatric drugs, such as thioridazine, as analgesics for burns, sun burns, and freezing injuries by interfering with the action of the "calcium-calmodulin complex." Beitner mentions the topical anesthetic agent lidocaine hydrochloride in an amount of 0.1 - 10 wt% as an adjuvant in the study. However, Beitner neither teaches nor suggests a composition having two barrier gels that provides ideal conditions for skin epithelium regeneration; helps to remove debris and necrotic tissues; prevents tissue mistreatment during intervention by not adhering to the injury; suppresses local pain in the injury by creating a cover over nerve endings; creates a protecting defense barrier for the body by isolating the injury from contamination sources; prevents the accumulation of secretions in the injury; prevents wound dehydration due to water evaporation; removes bacteria by virtue of its antiseptic component; and creates a rapid epithelialization process, thus decreasing scar formation.

Chen – Chen fails to teach or suggest the features of the invention that are omitted from Klein, Parrilla and Beitner. Chen teaches a topical spray for the treatment of burns that incorporates chlorhexidine in an amount of 0.05 - 10 wt%. Chen describes chlorhexidine as an antiseptic and disinfecting agent effective against a wide range of bacteria, certain fungi, and certain viruses. Chen mentions preparations with the anti-infectious properties owing to chlorhexidine.

However, Chen similarly fails to teach a composition having two barrier gels that provides ideal conditions for skin epithelium regeneration; promotes the elimination of debris and necrotic tissues; prevents tissue mistreatment during interventions by not adhering to the injury; prevents stress to the patient and his/her tissues by suppressing pain and, thus prevents autonomic, somatic, and endocrine responses; suppresses local pain of the injury through two mechanisms: covering nerve endings and analgesic action; creates a protecting defense barrier for the body, thus isolating the injury from contamination sources; prevents the accumulation of

secretions in the injury; prevents wound dehydration due to water evaporation and creates a rapid epithelialization process, thus decreasing scar formation.

Response to Arguments

In reply to the Examiner's Response beginning on page 10 of the outstanding Office Action, Applicant acknowledges the Examiner's request for objective evidence that the present invention has unexpected properties. Enclosed herewith is a 37 CFR § 1.132 Declaration of Harold Armando Gomez Torres, the present inventor. The Examiner is respectfully requested to review the enclosed Declaration of Dr. Gomez Torres as it provides strong evidence of the patentability of the present invention.

Relevant to this § 103(a) rejection, *Graham v. John Deere*, 383 U.S. 1, 17, 148 USPQ 459, 467 (1966) has provided the controlling framework for an obviousness analysis, wherein a proper analysis under § 103(a) requires consideration of the four *Graham* factors. One such factor includes the evaluation of any evidence of secondary considerations (e.g., commercial success; unexpected results). 383 U.S. at 17, 148 USPQ at 467. In this regard, Applicant respectfully submits that the present invention has achieved unexpected results, whereby such results rebut any asserted *prima facie* case of obviousness. *See In re Corkill*, 711 F.2d 1496, 226 USPQ 1005 (Fed. Cir. 1985). Also, the comparative showing need not compare the claimed invention with all of the cited prior art, but only with the closest prior art. *See* MPEP 716.02(b) and 716.02(e).

According to MPEP 2145, rebuttal evidence and arguments can be presented by way of an affidavit or declaration under 37 CFR 1.132, *In re Soni*, 54 F.3d 746, 750, 34 USPQ2d 1684, 1687 (Fed. Cir. 1995). Office personnel should consider all rebuttal arguments and evidence presented by Applicants. See, e.g., *In re Piasecki*, 745 F.2d 1468, 1472, 223 USPQ 785, 788 (Fed. Cir. 1984) ("[Rebuttal evidence] may relate to any of the *Graham* factors including the so-called secondary considerations."). Rebuttal evidence may also include evidence that the claimed invention yields unexpectedly improved properties or properties not present in the prior art. Rebuttal evidence may consist of a showing that the claimed compound possesses unexpected properties. *In re Dillon*, 919 F.2d 688, 692-93, 16 USPQ2d 1897, 1901 (Fed. Cir. 1990).

As stated in *KSR International Co. v Teleflex Inc.*, 82 USPQ2d 1385, 1396 (2007), "rejections on obviousness cannot be sustained by mere conclusory statements; instead, there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness." Furthermore, the mere fact that references ***can*** be combined or modified does not render the resultant combination obvious unless the results would have been predictable to one of ordinary skill in the art. *Id.* As described above, Applicant has shown that the present invention achieves unexpected and unpredictable results.

Furthermore, Applicant respectfully submits that the Examiner did not respond to the barrier effect of the present invention. In the combination of Klein and Parrilla, there is no barrier effect as a therapeutic method. However, the Examiner appears to assert that carbopol is disclosed in Klein as a therapeutic agent. However, the composition of Klein does not offer a barrier effect. Rather, the composition is a lubricant, softener, cleaner, and anti-pruritic preparation.

The combination of Klein and Parrilla does not disclose the amount of carboxypolymehtylene for obtaining a "therapeutic action" as claimed in the present invention.

Finally, the Examiner asserts that parabens are antimicrobial agents. However, parabens are stabilizers effective against fungi and yeast, and they are used as antimicrobial preservatives in the preparation of cosmetics and food. Consequently, parabens are not specific substances for the treatment of infections.

Summary

To establish a *prima facie* case of obviousness of a claimed invention, all of the claim limitations must be disclosed by the cited references. As discussed above, Klein in view of the secondary references fail to disclose all of the claim limitations of independent claim 1, and those claims dependent thereon. Accordingly, the combination of references does not render the present invention obvious.

Furthermore, the cited references or the knowledge in the art provide no reason or rationale that would allow one of ordinary skill in the art to arrive at the present invention as claimed. Therefore, a *prima facie* case of obviousness has not been established, and withdrawal

of the outstanding rejection is respectfully requested. Any contentions of the USPTO to the contrary must be reconsidered at present.

Distinctions over CO '011 in view of the secondary references

CO '011 simply reveals information related to skin anatomy, physiology, a table on the types of burns and avulsions (epidemiology, pathophysiology, depth, etiology, physical and chemical agents, radiation, biological agents, animals, frostbite, burns, etc.). In other words, CO '011 provides only a theoretical framework.

Although CO '011 defines in part a gel, the reference mainly addresses the definition of the components as usually employed in the state of the art. Accordingly, this document includes the carboxymethylcellulose, carbopol and papain and a couple of examples presented as "claims." Although the reference includes the components mentioned by the Examiner, among them methyl and propyl paraben, they are not properly supported in the description, and one of ordinary skill in the art does not find clear teachings or suggestions from these "claims-examples" that would motivate him or her to arrive at the claimed composition. Additionally, CO '011 does not disclose the chlorhexidine as an antiseptic or urea as a lubricating agent as applied in the present invention.

Additionally, Applicant respectfully submits that the Examiner has misinterpreted the use of analgesics and antibiotics in the gel described in CO '011. Specifically, page 8 of this reference states [prodegel is the name employed for the gel]:

> *Small Burns*
>
> [...]
>
> *In this case, the hydroelectrolytic, immune and vascular systems of the patient are not affected, the injury is not infected (unless it has more than 3 days), neither the surrounding tissues are infected, in such manner that the treatment focuses on preventing superinfection, fluid loss, injury cleaning, treatment of inflammation of the area, analgesia and covering the burned area to protect it from any form of aggression of the environment. Prodegel is designed for the local treatment of burns.*
>
> *If a burn is small, not deep and not complicated, the treatment comprises covering, cleaning, examining, washing, treating pain and debriding the area, in this manner the infection is prevented and there is re-epithelialization and complete healing within a*

maximum period of 3 to 5 days, avoiding the use of painkillers, antibiotic substances, and other products for local covering. (Emphasis added).

As such, CO '011 expressly teaches away from the claimed subject matter regarding the use of analgesics within the composition. In fact, excerpts on page 9 teach away from the present invention with respect to the use of these components:

It is important to recognize that topical antibiotic therapy is designed to control the burn sepsis and not for routine treatment of minor burns in which sepsis is not the problem. (Emphasis added).

Furthermore, pages 9 and 10 mention some of the antibiotics that have generally been used to treat burns but indicate the disadvantages thereof:

The use of topical antibiotic therapy in burns was not designed to treat superficial lesions which treatment is very different and explains the use of prodegel. Local antibiotic therapy should be reserved for those clinical instances in which the burn sepsis will be a significant problem. The superficial burn patient will not benefit from the use of antibiotics (emphasis added).

According to the above, the gel described in CO '011 is not indicated for the treatment of infections. Rather, it only prevents superinfection. Similarly, among the advantages cited for the gel of CO '011, the analgesic effect is not mentioned (see pages 13 and 14). The reference neither indicates nor exemplifies analgesics that could be employed in the composition.

As described above, the claimed composition provides an unexpected therapeutic effect resulting from the combination of the two specific gels in addition to a barrier, antiseptic, anti-inflammatory and debriding effect.

As discussed above, CO '011 does not disclose each and every aspect of the pending claims. Applicants respectfully submit that the secondary references do not overcome the deficiencies of this reference.

To establish a *prima facie* case of obviousness of a claimed invention, all of the claim limitations must be disclosed by the cited references. As discussed above, CO '011 in view of the secondary references fail to disclose all of the claim limitations of independent claim 1, and those claims dependent thereon. Accordingly, the combination of references does not render the present invention obvious.

Furthermore, the cited references or the knowledge in the art provide no reason or rationale that would allow one of ordinary skill in the art to arrive at the present invention as claimed. Therefore, a *prima facie* case of obviousness has not been established, and withdrawal of the outstanding rejection is respectfully requested. Any contentions of the USPTO to the contrary must be reconsidered at present.

Conclusion

All of the stated grounds of rejection have been properly traversed, accommodated, or rendered moot. Applicant therefore respectfully requests that the Examiner reconsider all presently outstanding rejections and that they be withdrawn. It is believed that a full and complete response has been made to the outstanding Office Action, and as such, the present application is in condition for allowance.

Should there be any outstanding matters that need to be resolved in the present application, the Examiner is respectfully requested to contact MaryAnne Armstrong, PhD, Registration No. 40,069, at the telephone number of the undersigned below to conduct an interview in an effort to expedite prosecution in connection with the present application.

If necessary, the Director is hereby authorized in this, concurrent, and future replies to charge any fees required during the pendency of the above-identified application or credit any overpayment to Deposit Account No. 02-2448.

Dated: November 24, 2010

Respectfully submitted,

By _____

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Attachment: 37 CFR § 1.132 Declaration of Harold Armando Gomez Torres